



## SIX3 gene

SIX homeobox 3

### Normal Function

The *SIX3* gene provides instructions for making a protein that plays an important role in the development of the eyes and front part of the brain (forebrain). This protein is a transcription factor, which means that it attaches (binds) to specific regions of DNA and helps control the activity of certain genes. The *SIX3* protein regulates genes involved in several signaling pathways that are important for embryonic development. Some of these genes are turned on (activated) by the *SIX3* protein and others are turned off (repressed).

One gene that is activated by the *SIX3* protein is the *SHH* gene, which provides instructions for making a protein called Sonic Hedgehog. Among its many functions, Sonic Hedgehog helps establish the right and left halves (hemispheres) of the forebrain. The *SIX3* protein also regulates genes involved in the formation of the lens of the eye and the specialized tissue at the back of the eye that detects light and color (the retina).

### Health Conditions Related to Genetic Changes

#### nonsyndromic holoprosencephaly

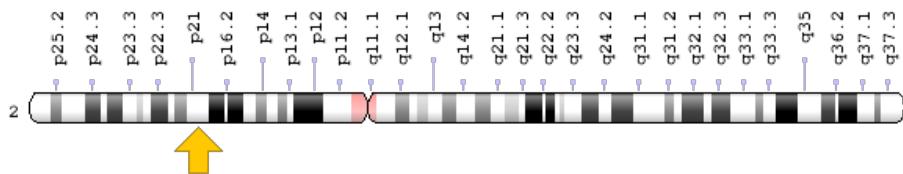
At least 60 mutations in the *SIX3* gene have been found to cause nonsyndromic holoprosencephaly. This condition occurs when the brain fails to divide into two hemispheres during early development. *SIX3* gene mutations are the third most common cause of nonsyndromic holoprosencephaly. Although mutations in this gene can cause mild to severe forms of the condition, they tend to result in more severe signs and symptoms than mutations in other genes that cause nonsyndromic holoprosencephaly.

*SIX3* gene mutations change the structure of the *SIX3* protein in different ways; however, all of them disrupt the protein's ability to bind with DNA. As a result, the genes involved in normal eye and forebrain development are not properly activated or repressed. Without the correct activity of these genes, the eyes will not form normally and the brain does not separate into two hemispheres. The signs and symptoms of nonsyndromic holoprosencephaly are caused by abnormal development of the brain and face.

## Chromosomal Location

Cytogenetic Location: 2p21, which is the short (p) arm of chromosome 2 at position 21

Molecular Location: base pairs 44,941,898 to 44,946,077 on chromosome 2 (Homo sapiens Annotation Release 108, GRCh38.p7) (NCBI)



Credit: Genome Decoration Page/NCBI

## Other Names for This Gene

- homeobox protein SIX3
- HPE2
- sine oculis homeobox homolog 3
- SIX3\_HUMAN

## Additional Information & Resources

### Educational Resources

- Developmental Biology (sixth edition, 2000): The Dynamics of Optic Development  
<https://www.ncbi.nlm.nih.gov/books/NBK10024/#A2921>
- Developmental Biology (sixth edition, 2000): The Hedgehog Pathway  
<https://www.ncbi.nlm.nih.gov/books/NBK10043/#A1063>

### GeneReviews

- Holoprosencephaly Overview  
<https://www.ncbi.nlm.nih.gov/books/NBK1530>

### Scientific Articles on PubMed

- PubMed  
<https://www.ncbi.nlm.nih.gov/pubmed?term=%28SIX3%5BTIAB%5D%29+AND+%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1800+days%22%5Bdp%5D>

## OMIM

- SINE OCULIS HOMEOBOX, DROSOPHILA, HOMOLOG OF, 3  
<http://omim.org/entry/603714>

## Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology  
[http://atlasgeneticsoncology.org/Genes/GC\\_SIX3.html](http://atlasgeneticsoncology.org/Genes/GC_SIX3.html)
- ClinVar  
<https://www.ncbi.nlm.nih.gov/clinvar?term=SIX3%5Bgene%5D>
- HGNC Gene Family: SINE class homeoboxes  
<http://www.genenames.org/cgi-bin/genefamilies/set/525>
- HGNC Gene Symbol Report  
[http://www.genenames.org/cgi-bin/gene\\_symbol\\_report?q=data/hgnc\\_data.php&hgnc\\_id=10889](http://www.genenames.org/cgi-bin/gene_symbol_report?q=data/hgnc_data.php&hgnc_id=10889)
- NCBI Gene  
<https://www.ncbi.nlm.nih.gov/gene/6496>
- UniProt  
<http://www.uniprot.org/uniprot/O95343>

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